

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 1 225 225 A3

(12)

## EUROPEAN PATENT APPLICATION

(88) Date of publication A3:  
08.01.2003 Bulletin 2003/02

(51) Int Cl.7: C12N 15/12, C07K 14/51,  
A61K 38/18, A61L 27/22,  
A61L 27/54

(43) Date of publication A2:  
24.07.2002 Bulletin 2002/30

(21) Application number: 01201546.7

(22) Date of filing: 07.04.1989

(84) Designated Contracting States:  
AT BE CH DE FR GB IT LI LU NL SE

(30) Priority: 08.04.1988 US 179406  
15.08.1988 US 232630  
23.02.1989 US 315342

(62) Document number(s) of the earlier application(s) in  
accordance with Art. 76 EPC:  
95201872.9 / 0 714 665  
89904986.0 / 0 362 367

(71) Applicant: STRYKER CORPORATION  
Kalamazoo, Michigan 49003-4085 (US)

(72) Inventors:

- Kuberasampath, Thangavel  
Holliston, MA 01746 (US)
- Oppermann, Hermann  
Medway, Massachusetts 02053 (US)
- Rueger, David C.  
West Roxbury, Massachusetts 02132 (US)
- Ozkaynak, Engin  
Milford, Massachusetts 01757 (US)

(74) Representative: Hutchins, Michael Richard et al  
FRY HEATH & SPENCE LLP  
The Old College  
53 High Street  
Horley Surrey RH6 7BN (GB)

(54) Osteogenic devices

(57) Disclosed are 1) osteogenic devices comprising a matrix containing osteogenic protein and methods of inducing endochondral bone growth in mammals using the devices; 2) amino acid sequence data, amino

acid composition, solubility properties, structural features, homologies and various other data characterizing osteogenic proteins, and 3) methods of producing osteogenic proteins using recombinant DNA technology.

FIG. 1A-1

```

10      20      30      40      50      60      70
GGAGGTATAGGAGCTCTCTCGATTTTAGCAAAACAGGAGTCCGAAGATCTAAGGAGAGCTGGGGGTTTGACTCC
      SacI
85      95      105     115     125     135     145
GAGAGCTCGAGCAGTCCCAAGACCTGGTCTTGACTCAGAGTTAGACTCCACTCAGAGGCTGACTGTCTCCAGG
      SacI      PflMI
160     170     180     190     200     210     220
GTCTACACCTCTAAGGGCGACACTGGGCTCAAGCAGACTGCCGTTTCTATATGGGATGAGCCTTCACAGGGCAG
      235     245     255     265     275     285     295
CCAGTTGGGATGGCTTGAGCTTTGGCTGTAGACATCAGAAACCAAGTCAATGCGCTTCAACAGTAGAAAAAT
      310     320     330     340     350     360     370
CACCAGCCCGCAGAGCTAAGGTTGGGTGGACATTAGGTTGGTTGATCCAGGAGCTCAACAGTGTCTCTGAGCC
      385     395     405     415     425     435     445
CCAGCTCCTTCTGCCCAACCCACCATCTTCAGTGTCTCTCTCAAGGCCACAGCTGTAGTTGGCCAGGGGG
      PvuII      BclI
460     470     480     490     500     510     520
GCTTCATTATTTTGGCTCCTGGGCACTAGGAGGAAGAGAATGATGCTCTCCATGGGTCTTCTTAGGAATGT
      NcoI
535     545     555     565     575     585     595
GGGAACCTTTTCCAGAAGTCTCTATGCTTTTAGTTTGTGTTGGGTCACTTGGCCTTCTCAACCACTTCCTGAC
      610     620     630     640     650     660     670
TCTCGGACAGGATGTGCACCTGATGACCTTAGCTTTGGGATCTAATAGTCACTTTACAAAGCCTCTTTGAGAAG
      ApaLI      EspI
685     695     705     715     725     735     745
TGACATTGGAACCAAGCTTGAGCAGACACAAAGATTGCAGGGAGGGCATTGCAGGTGGAGGAAACGGCAC
      BspMI-
760     770     780     790     800     810     820
ATGCAAGAGCCCTGCGTGGGAGTGAGCTTGGTGTGTTGGTCAATCACTTGTACAGACACACGGGCGCTGTACGA
      ApaI      EcoRI

```

EP 1 225 225 A3



FIG. 1A-6

4585 4595 4605 4615 4625 4635 4645  
 CTGCAGTCATTTCATTATGCCAGACAGGATGTTTCTTTATAGAAACGTGGAGGCCAGTTAGAACGACTCACCGCT  
 pMI+  
 PstI  
 4660 4670 4680 4690 4700 4710 4720  
 TCTCACCAGTCCCCATGTTTGGTGTGTGTTTCAGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCT  
 PflMI  
 4735 4745 4755 4765 4775 4785 4795  
 GTGCGCCACGCAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA  
 4810 4820 4830 4840  
 GAAACATGGTGGTCCGGGCTGTGGCTGCCACTAGCTCCTCCGA

FIG. 1B

CONSENSUS PROBE 20 30 40 50 60 70  
 GATCCTAATGGGCTGTACGTGGACTTCCAGCGGACGTGGGCTGGGACGACTGGATCATCGCCCCGTCG  
 \*\* \*\* \* \* \* \* \*  
 TGTAAGAAGCAGCAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCTGAAG  
 OP4 28 38 48 58 68 78 88  
 80 90 100 110 120 130 140  
 ACTTCGACGCCTACTACTGCTCCGAGCCTGCCAGTTCCCTCTGCGGATCACTTCAACAGCACCAACCA  
 \*\* \* \* \* \* \*  
 GCTACGCGCGCTACTACTGTGAGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCA  
 98 108 118 128 138 148 158  
 150 160 170 180 190 200 210  
 CGCCGTGGTGCAGACCCCTGGTGAACAACATGAACCCCGCAAGGTACCCAAGCCCTGCTGCGTGCCCAACC  
 \*\*\*\* \* \* \* \* \*  
 CGCCATCGTGCAGACGCTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCACG  
 168 178 188 198 208 218 228  
 220 230 240 250 260 270 280  
 GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGCTGAAGAACTACCAGGAGA  
 \*\*\*\* \* \* \* \* \*  
 CAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA  
 238 248 258 268 278 288 298  
 290 300 310  
 TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA  
 \*\* \* \* \* \* \*  
 TGGTGGTCCGGGCTGTGGCTGCCACTAGCTCCT  
 308 318 328



European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 1546

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
D,X	WO 88 00205 A (GENETICS INST) 14 January 1988 (1988-01-14) * the whole document *	1-7,9-15	C12N15/12 C07K14/51 A61K38/18 A61L27/22 A61L27/54
D,X	EP 0 148 155 A (DOW CHEMICAL CO) 10 July 1985 (1985-07-10) * the whole document *	1-4, 11-15	
X	URIST M R ET AL.: "Preparation and bioassay of bone morphogenetic protein and polypeptide fragments" METHODS IN ENZYMOLOGY, vol. 146, 1987, pages 294-312, XP000565634 * the whole document *	1-4, 11-15	
D,X	URIST M R ET AL.: "Purification of bovine bone morphogenetic protein by hydroxyapatite chromatography." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 81, no. 2, January 1984 (1984-01), pages 371-375, XP002198250 ISSN: 0027-8424 * the whole document *	1-4, 11-15	
A	EP 0 169 016 A (COLLAGEN CORP) 22 January 1986 (1986-01-22) * the whole document *	1-4	
A	EP 0 182 483 A (COLLAGEN CORP) 28 May 1986 (1986-05-28) * the whole document *	1-4, 11-15	
-/--			
-The present search report has been drawn up for all claims			
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>14 May 2002</b>	Examiner <b>van de Kamp, M</b>
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1503 03/82 (P04/C01)



European Patent  
Office

Application Number

EP 01 20 1546

### CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

### LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-15 (all partially)



European Patent  
Office

## EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 1546

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
A	URIST M R ET AL.: "Beta-tricalcium phosphate delivery system for bone morphogenetic protein" CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, PHILADELPHIA, PA, US, vol. 187, July 1984 (1984-07), pages 277-280, XP008003034 * the whole document *	11-15	
A	RUEGER J M ET AL.: "Implant materials for bone-replacement. Comparison of the osteostimulative property of four different agents and their combinations by orthotopic implantation in dogs" CALCIFIED TISSUE INTERNATIONAL, vol. 36, no. SUPPL. 2, 1984, page S69 XP008003109 ISSN: 0171-967X * the whole document *	11-15	
A	PADGETT R W ET AL.: "A transcript from a Drosophila pattern gene predicts a protein homologous to the transforming growth factor-beta family" NATURE, vol. 325, 1987, pages 81-84, XP002036812 ISSN: 0028-0836 * the whole document *	3,4,8	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
A	WEEKS D L ET AL.: "A maternal mRNA localized to the vegetal hemisphere in Xenopus eggs codes for a growth factor related to TGF-beta" CELL, vol. 51, 4 December 1987 (1987-12-04), pages 861-867, XP000653563 ISSN: 0092-8674 * the whole document *	3,4,8	
-/--			
-The present search report has been drawn up for all claims			
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>14 May 2002</b>	Examiner <b>van de Kamp, M</b>
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1503 03/82 (P/AC01)



European Patent  
Office

LACK OF UNITY OF INVENTION  
SHEET B

Application Number  
EP 01 20 1546

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-15 (all partially)

Use of a composition consisting of a single species of osteogenic protein as active osteogenic ingredient, said protein comprising of an unpaired polypeptide chain or which protein does not comprise a pair of polypeptide chains and is capable of inducing endochondral bone formation when disposed within a matrix and implanted in a mammal, for the manufacture of a medicament for inducing endochondral bone formation, wherein the protein comprises the sequence VPKPCCAPT or LYCSF-to-ACGHC or HQRQA-to-ACGHC (according to claim 8a-c). Said osteogenic protein in unglycosylated form, a process for its production, and a polypeptide producible by said process. Said use, protein, process or polypeptide wherein the protein has an apparent molecular weight of 30 kD in the glycosylated native form (27 kD in deglycosylated form), or comprises two polypeptide chains with apparent molecular weights of 16 and 18 kD in glycosylated form (14 to 16 kD in glycosylated form). Processes for producing an osteogenic device comprising disposing said protein in a matrix, for implantation in a mammal.

2. Claims: 1-15 (all partially)

Use of a composition consisting of a single species of osteogenic protein as active osteogenic ingredient, said protein comprising of an unpaired polypeptide chain or which protein does not comprise a pair of polypeptide chains and is capable of inducing endochondral bone formation when disposed within a matrix and implanted in a mammal, for the manufacture of a medicament for inducing endochondral bone formation, wherein the protein comprises the sequence CKRHP-to-GCGCR (according to claim 8d). Said osteogenic protein in unglycosylated form, a process for its production, and a polypeptide producible by said process. Said use, protein, process or polypeptide wherein the protein has an apparent molecular weight of 30 kD in the glycosylated native form (27 kD in deglycosylated form), or comprises two polypeptide chains with apparent molecular weights of 16 and 18 kD in glycosylated form (14 to 16 kD in glycosylated form). Processes for producing an osteogenic device comprising disposing said protein in a matrix, for implantation in a mammal.

3. Claims: 1-15 (all partially)

Use of a composition consisting of a single species of osteogenic protein as active osteogenic ingredient, said protein comprising of an unpaired polypeptide chain or which



European Patent  
Office

LACK OF UNITY OF INVENTION  
SHEET B

Application Number  
EP 01 20 1546

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

protein does not comprise a pair of polypeptide chains and is capable of inducing endochondral bone formation when disposed within a matrix and implanted in a mammal, for the manufacture of a medicament for inducing endochondral bone formation, wherein the protein comprises the sequence CRRHS-to-GCGCR (according to claim 8e). Said osteogenic protein in unglycosylated form, a process for its production, and a polypeptide producible by said process. Said use, protein, process or polypeptide wherein the protein has an apparent molecular weight of 30 kD in the glycosylated native form (27 kD in deglycosylated form), or comprises two polypeptide chains with apparent molecular weights of 16 and 18 kD in glycosylated form (14 to 16 kD in glycosylated form). Processes for producing an osteogenic device comprising disposing said protein in a matrix, for implantation in a mammal.

4. Claims: 1-15 (all partially)

Use of a composition consisting of a single species of osteogenic protein as active osteogenic ingredient, said protein comprising of an unpaired polypeptide chain or which protein does not comprise a pair of polypeptide chains and is capable of inducing endochondral bone formation when disposed within a matrix and implanted in a mammal, for the manufacture of a medicament for inducing endochondral bone formation, wherein the protein comprises the sequence CARRY-to-SCACR (according to claim 8f). Said osteogenic protein in unglycosylated form, a process for its production, and a polypeptide producible by said process. Said use, protein, process or polypeptide wherein the protein has an apparent molecular weight of 30 kD in the glycosylated native form (27 kD in deglycosylated form), or comprises two polypeptide chains with apparent molecular weights of 16 and 18 kD in glycosylated form (14 to 16 kD in glycosylated form). Processes for producing an osteogenic device comprising disposing said protein in a matrix, for implantation in a mammal.





European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 1546

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
A	URIST M R ET AL.: "Bone cell differentiation and growth factors" SCIENCE (WASHINGTON D C), vol. 220, no. 4598, 1983, XP008003037 ISSN: 0036-8075 * the whole document *		
D,P, X	WANG E A ET AL.: "Purification and characterization of other distinct bone-inducing factors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 85, no. 24, 1 December 1988 (1988-12-01), pages 9484-9488, XP000008758 ISSN: 0027-8424 * the whole document *	3,4,9	
E	WO 90 11366 A (GENETICS INST) 4 October 1990 (1990-10-04) * the whole document *	1-4,7-9, 11-15	
T	OZKAYNAK E ET AL.: "OP-1 cDNA encodes an osteogenic protein in the TGF-beta family" EMBO JOURNAL, vol. 9, no. 7, 1 July 1990 (1990-07-01), pages 2085-2093, XP000611252 ISSN: 0261-4189 * the whole document *		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
-The present search report has been drawn up for all claims			
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>14 May 2002</b>	Examiner <b>van de Kamp, M</b>
<p><b>CATEGORY OF CITED DOCUMENTS</b></p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons &amp; : member of the same patent family, corresponding document</p>			

EPO FORM 1603 03.02 (p04001)



European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 01 20 1546

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
T	SAMPATH T K ET AL.: "Bovine osteogenic protein is composed of dimers of OP-1 and BMP-2a, two members of the transforming growth factor-beta superfamily" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 265, no. 22, 5 August 1990 (1990-08-05), pages 13198-13205, XP000611250 ISSN: 0021-9258 * the whole document *		
T	CELESTE A J ET AL.: "Identification of transforming growth factor beta family members present in bone-inductive protein purified from bovine bone" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 87, no. 24, 1 December 1990 (1990-12-01), pages 9843-9847, XP000168624 ISSN: 0027-8424 * the whole document *		
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
<del>The present search report has been drawn up for all claims</del>			
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>14 May 2002</b>	Examiner <b>van de Kamp, M</b>
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons * : member of the same patent family, corresponding document	

EPO FORM 1503 (03.02 (P04C01))

# ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

EP 01 20 1546

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-05-2002

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8800205 A	14-01-1988	US 4877864 A	31-10-1989
		AT 141928 T	15-09-1996
		AU 613314 B2	01-08-1991
		AU 7783587 A	29-01-1988
		DE 3751887 D1	02-10-1996
		DE 3751887 T2	06-03-1997
		DK 53497 A	09-05-1997
		DK 106288 A	28-04-1988
		EP 1254956 A2	06-11-2002
		EP 0313578 A1	03-05-1989
		EP 0688869 A1	27-12-1995
		ES 2007625 A6	01-07-1989
		GR 871028 A1	11-01-1988
		IE 75881 B1	24-09-1997
		IE 970378 L	01-01-1988
		IL 83003 A	31-07-1995
		JP 2729222 B2	18-03-1998
		JP 6298800 A	25-10-1994
		JP 3093682 B2	03-10-2000
		JP 10070989 A	17-03-1998
		JP 2500241 T	01-02-1990
		JP 2713715 B2	16-02-1998
		KR 9705583 B1	18-04-1997
		MX 170919 B	22-09-1993
		NZ 220894 A	28-05-1990
		PT 85225 A ,B	01-08-1987
		WO 8800205 A1	14-01-1988
		US 5543394 A	06-08-1996
		US 5631142 A	20-05-1997
		US 5013649 A	07-05-1991
		US 6207813 B1	27-03-2001
		US 5459047 A	17-10-1995
		US 5166058 A	24-11-1992
		US 5635373 A	03-06-1997
		US 5849880 A	15-12-1998
		US 5187076 A	16-02-1993
		US 6432919 B1	13-08-2002
		US 5618924 A	08-04-1997
		US 5116738 A	26-05-1992
		US 6150328 A	21-11-2000
		US 5366875 A	22-11-1994
		US 5939388 A	17-08-1999
		US 2002061577 A1	23-05-2002
		US 6245889 B1	12-06-2001
		US 6177406 B1	23-01-2001
		NO 880701 A	17-02-1988

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 01 20 1546

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-05-2002

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 8800205	A		NO 963788 A	17-02-1988
			NO 963789 A	17-02-1988
			US 5106748 A	21-04-1992
			US 5108922 A	28-04-1992
-----				
EP 0148155	A	10-07-1985	AT 42309 T	15-05-1989
			AU 580975 B2	09-02-1989
			AU 3722184 A	11-07-1985
			CA 1241641 A1	06-09-1988
			DE 3569542 D1	24-05-1989
			DK 2285 A ,B,	05-07-1985
			EP 0148155 A2	10-07-1985
			GR 850006 A1	03-05-1985
			IE 57966 B1	02-06-1993
			JP 60226814 A	12-11-1985
			NZ 210699 A	28-06-1989
			US 4804744 A	14-02-1989
			ZA 8500047 A	24-09-1986
-----				
EP 0169016	A	22-01-1986	AT 128715 T	15-10-1995
			AU 592951 B2	01-02-1990
			AU 4501585 A	23-01-1986
			AU 594949 B2	22-03-1990
			AU 5649586 A	29-10-1987
			CA 1261549 A1	26-09-1989
			DE 3588058 D1	09-11-1995
			DE 3588058 T2	02-05-1996
			EP 0169016 A2	22-01-1986
			JP 2074953 C	25-07-1996
			JP 7094474 B	11-10-1995
			JP 61036223 A	20-02-1986
			US 4774322 A	27-09-1988
			US 4774228 A	27-09-1988
			US 4810691 A	07-03-1989
			US 4843063 A	27-06-1989
			US RE35694 E	16-12-1997
			US RE34090 E	06-10-1992
-----				
EP 0182483	A	28-05-1986	US 4563350 A	07-01-1986
			AT 54830 T	15-08-1990
			AU 585268 B2	15-06-1989
			AU 4900585 A	01-05-1986
			CA 1266613 A1	13-03-1990
			DE 3578874 D1	30-08-1990
			EP 0182483 A1	28-05-1986
			JP 1855544 C	07-07-1994

EPO FORM P0419

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 01 20 1546

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-05-2002

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0182483	A		JP 5055149 B	16-08-1993
			JP 62016421 A	24-01-1987
			US 4888366 A	19-12-1989
			US 5001169 A	19-03-1991
-----				
WO 9011366	A	04-10-1990	US 5106748 A	21-04-1992
			US 5141905 A	25-08-1992
			US 5187076 A	16-02-1993
			AT 162223 T	15-01-1998
			AU 624940 B2	25-06-1992
			AU 5357790 A	22-10-1990
			CA 2030518 A1	29-09-1990
			DE 69031939 D1	19-02-1998
			DE 69031939 T2	10-09-1998
			DK 429570 T3	27-04-1998
			EP 0429570 A1	05-06-1991
			ES 2113857 T3	16-05-1998
			JP 3505098 T	07-11-1991
			KR 214740 B1	02-08-1999
			KR 239203 B1	15-01-2000
			KR 247216 B1	15-03-2000
			WO 9011366 A1	04-10-1990
			US 5543394 A	06-08-1996
			US 6207813 B1	27-03-2001
			US 5635373 A	03-06-1997
			US 5366875 A	22-11-1994
			US 5939388 A	17-08-1999
			US 2002061577 A1	23-05-2002
			US 5459047 A	17-10-1995
			US 5849880 A	15-12-1998
			MX 9203129 A1	01-07-1992
			MX 9203296 A1	01-07-1992
			MX 9203127 A1	01-07-1992
-----				

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82